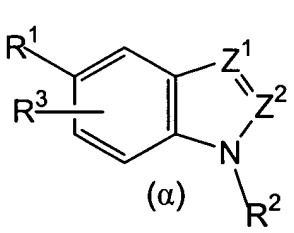
Claims

1. A compound of the formula:



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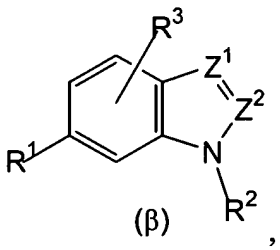


,

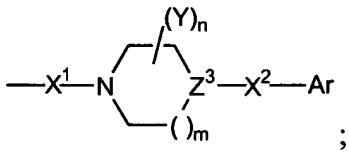
and the pharmaceutically acceptable salts thereof,

wherein each of Z^1 and Z^2 is independently CR^4 or N;

where each R^4 is independently H or is alkyl (1-6C) or aryl, each of said alkyl or aryl optionally including one or more heteroatoms selected from O, S and N and optionally substituted by one or more of halo, OR, SR, NR_2, RCO, COOR, $CONR_2$, OOCR, or NROCR where R is H or alkyl (1-6C), or by one or more CN or =O, or by one or more aliphatic or aromatic 5- or 6-membered rings optionally containing 1-2 heteroatoms; or

two R^4 taken together form a bridge optionally containing a heteroatom;

R^1 is



;

wherein

X^1 is CO or an isostere thereof;

m is 0 or 1;

Y is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl or two Y taken together may form an alkylene (2-3C) bridge;

n is 0, 1 or 2;

Z^3 is CH or N;

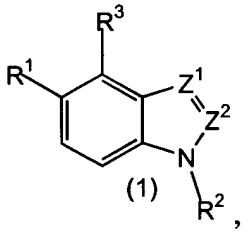
X^2 is CH, CH_2 or an isostere thereof; and

Ar consists of one or two phenyl moieties directly coupled to X^2 optionally substituted by halo, nitro, alkyl (1-6C), alkenyl (1-6C), alkynyl (1-6C), CN or CF_3, or by RCO, COOR, $CONR_2$, NR_2, OR, SR, OOCR or NROCR wherein R is H or alkyl (1-6C) or by phenyl, itself optionally substituted by the foregoing substituents;

R^2 is H, or is alkyl (1-6C) or aryl, each of said alkyl or aryl optionally including one heteroatom which is O, S or N, and optionally substituted by one or more of halo, OR, SR, NR_2, RCO, COOR, $CONR_2$, OOCR, or NROCR where R is H or alkyl (1-6C), or by one or more CN or =O, or by one or more aliphatic or aromatic 5- or 6-membered rings optionally containing 1-2 heteroatoms;

R^3 is H, halo, NO_2, alkyl (1-6C), alkenyl (1-6C), alkynyl (1-6C), CN, OR, SR, NR_2, RCO, COOR, $CONR_2$, OOCR, or NROCR where R is H or alkyl (1-6C).

2. The compound of claim 1 which is of the formula



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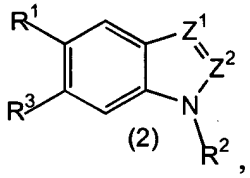

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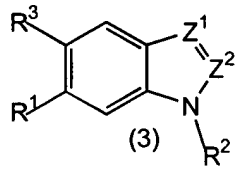

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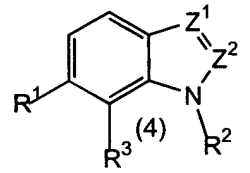


3. The compound of claim 1 wherein m is 1 and wherein n is 0.

4. The compound of claim 1 wherein X^1 is CO.

5. The compound of claim 1 wherein X^2 is CH_2.

6. The compound of claim 2 wherein n is 0, m is 1, X^1 is CO and X^2 is CH_2.

7. The compound of claim 1 wherein Z^1 and Z^2 are CR^4.

8. The compound of claim 6 wherein Z^1 and Z^2 are CR^4.

9. The compound of claim 1 wherein Z^1 is N and Z^2 is CH.

10. The compound of claim 6 wherein Z^1 is N and Z^2 is CH.

11. The compound of claim 2 which is of the formula (2).

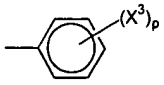
12. The compound of claim 6 which is of the formula (2).

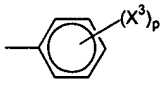
13. The compound of claim 2 wherein R^3 is halo or OR where R is alkyl (1-6C).

14. The compound of claim 6 wherein R^3 is halo or OR where R is alkyl (1-6C).

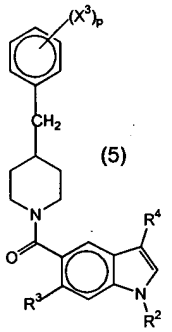
15. The compound of claim 1 wherein Z^3 is CH.

16. The compound of claim 6 wherein Z^3 is CH.

17. The compound of claim 1 wherein Ar is  wherein each X^3 is independently alkyl (1-6C), halo, OR, or NR_2 and p is 0, 1, 2 or 3.

18. The compound of claim 6 wherein Ar is  wherein each X^3 is independently alkyl (1-6C), halo, OR, or NR_2 and p is 0, 1, 2 or 3.

19. The compound of claim 6 which is of the formula:



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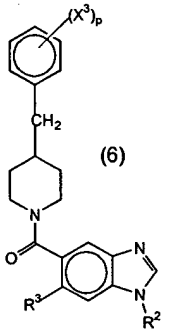


(6)

or having the structure of formula (5) or (6) wherein the positions on the indole or benzimidazole nucleus occupied by R^3 and the substituent illustrated as R^1 are reversed, wherein R^2, R^3 and R^4 are as defined in claim 1, and each X^3 is independently halo, alkyl (1-6C), OR, or NR_2, wherein R is H or alkyl (1-6C) and p is 0, 1, 2 or 3.

20. The compound of claim 19 wherein p is 0 or p is 1 or 2 and each X^3 is halo or OR where R is alkyl (1-3C).

21. The compound of claim 19 wherein R^4 is H or is of the formula CONY' wherein Y' is alkyl, aryl or arylalkyl optionally containing one or two heteroatoms.

22. The compound of claim 19 wherein R^2 is H.

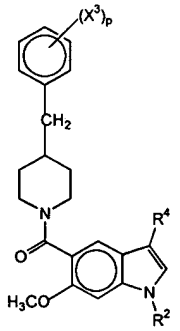
23. The compound of claim 19 wherein R^3 is H, halo, or OR, wherein R is alkyl (1-6C).

24. The compound of claim 23 wherein R^3 is chloro or methoxy.

25. The compound of claim 19 wherein the substituent R^1 shown in the 5-position of the indole or benzimidazole nucleus is at the 6-position and R^3 is at the 5-position.

26. The compound of claim 19 wherein the substituents in formulas (5) and (6) are in these positions as shown.

27. The compound of claim 19 which is of the formula



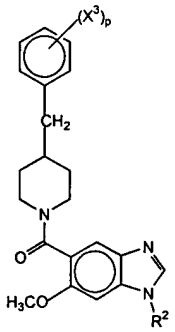
wherein R^2, R^4, X^3 and p are as defined in claim 19.

28. The compound of claim 27 wherein at least one of R^2 and R^4 is a polar group.

29. The compound of claim 27 wherein R^4 is H or is of the formula $R_2N(CH_2)_nNHCO$ wherein n is an integer of 1-3 and each R is independently H or alkyl

(1-6C) or wherein the Rs taken together form a ring optionally containing a heteroatom which is S, O or N.

30. The compound of claim 19 which is of the formula



wherein R^2, X^3 and p are as defined in claim 19.

31. The compound of claim 30 wherein R^2 is a polar group.

32. The compound of claim 29 wherein R^4 is H or is of the formula $R_2N(CH_2)_nNHCO$ wherein n is an integer of 1-3 and each R is independently H or alkyl (1-6C) or wherein the Rs taken together form a ring optionally containing a heteroatom which is S, O or N.

33. The compound of claim 1 which is

4-benzylpiperdinyl indole-5-carboxamide;

4-chloro-4-benzylpiperidinyl indole-5-carboxamide;

6-chloro-4-benzylpiperidinyl indole-5-carboxamide;

4-chloro-(4-(4-fluorobenzyl) piperidinyl)-indole-5-carboxamide;

6-chloro-(4-(4-fluorobenzyl) piperidinyl)-indole carboxamide;

4-methoxy-(4-benzylpiperidinyl)-indole-5-carboxamide;

6-methoxy-(4-benzylpiperidinyl)-indole-5-carboxamide;

4-methoxy-(4-(4-fluorobenzyl) piperidinyl)-indole-5-carboxamide;

6-methoxy-(4-(4fluorobenzyl) piperidinyl)-indole-5-carboxamide;

N-(3-cyclohexylmethylamino-2-hydroxypropyl)-(4-benzylpiperidinyl)-indole-5-carboxamide;

N-(3-N-methylpiperazinyl-2-hydroxypropyl)-(4-benzylpiperidinyl)-indole-5-carboxamide;

N-(3-benzylamino-2-hydroxypropyl)-(4-benzylpiperidinyl)-indole-5-carboxamide;

N-[3-{(4-methoxybenzyl)-amino}-2-hydroxypropyl-]-(4-benzylpiperidinyl)-indole-5-carboxamide;

N-{3-n-propylamino-2-hydroxypropyl}-(4-benzylpiperidinyl)-indole-5-carboxamide;

N-(4-pyridoyl)-(4-benzylpiperidinyl)indole-5-carboxamide;

N-(4-pyridylmethyl)-(4-benzylpiperidinyl)-indole-5-carboxamide;

N-methylacetyl-(4-benzylpiperidinyl)-indole-5-carboxamide;

N-acetyl-4-benzylpiperidinyl indole-5-carboxamide;

N-(n-propylamide)acetyl 4-benzylpiperidinyl indole-5-carboxamide;

4-benzylpiperidinyl-indole-5-carboxamide-1-acetic acid-n-butylamide;

4-benzylpiperidinyl-indole-5-carboxamide-1-acetic acid 4-methoxybenzyl amide;

3-(2-methoxyethylaminocarboxamidyl)-(4-benzylpiperidinyl)indole-5-carboxamide;

3-(2-methylaminoethylaminocarboxamidyl)-(4-benzylpiperidinyl)indole-5-carboxamide;

3-(2-aminoethylaminocarboxamidyl)-(4-benzylpiperidinyl)indole-5-carboxamide;

3-(4-benzylpiperidinylcarboxamidyl)-(4-benzylpiperidinyl)indole-5-carboxamide;

3-(4-benzylpiperidinylcarboxamidyl)-(4-benzylpiperidinyl)indole-6-carboxamide;

3-(4-fluorobenzylcarboxamidyl)-(4-benzylpiperidinyl)indole-5-carboxamide;

3-[2-(3,5-dimethoxyphenyl)ethylcarboxamidyl]-(4-benzylpiperidinyl)indole-5-carboxamide;

6-methoxy-(4-benzylpiperidinyl)indole-5-carboxamide;

3-trifluoroacetyl-(4-benzylpiperidinyl)indole-5-carboxamide;

6-methoxy-3-(2-dimethylaminoethylamino)carboxamidyl-(4-benzylpiperidinyl)indole-5-carboxamide;

3-trifluoroacetyl-4-benzylpiperidinylindole-5-carboxamide;

4-benzylpiperidinyl indole-5-carboxamide-3-carboxylic acid;

3-(2-dimethylamino)ethylaminocarboxamidyl-(4-benzylpiperidinyl)indole-5-carboxamide;

or is a compound as set forth in Table 5.

34. The compound of claim 32 which is

4-benzylpiperdinyl indole-5-carboxamide;

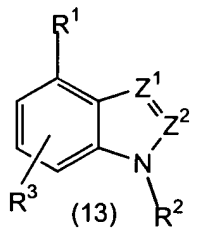
3-[2-dimethylaminoethylaminocarbonyl]-4-benzylpiperidinyl-6-methoxy indole-5-carboxamide; or

4-benzylpiperidinyl-6-methoxy benzimidazole-5-carboxamide.

35. A method to treat a condition characterized by a proinflammation response which method comprises administering to a subject in need of such treatment a compound of claim 1 or a pharmaceutical composition thereof.

36. The method of claim 35 wherein said condition characterized by inflammation is acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, uveitis, IBD, acute renal failure, head trauma, or ischemic/reperfusion injury.

37. A method to treat a heart condition associated with cardiac failure which method comprises administering to a subject in need of such treatment a compound of the formula



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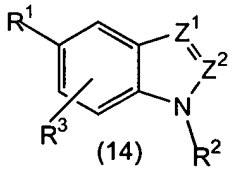
or



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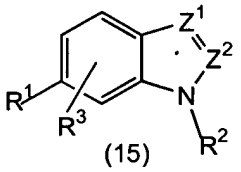

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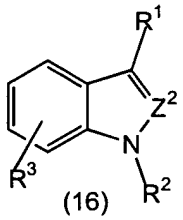
or



(16)

wherein R^1, R^2, R^3, Z^1, and Z^2 are as defined in claim 1, or administering a pharmaceutical composition thereof.

38. The method of claim 37 wherein said chronic heart condition is congestive heart failure, cardiomyopathy or myocarditis.